IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEBRASKA

CONSTANCE SUNDELL,

Plaintiff,

v.

NOVARTIS PHARMACEUTICALS CORPORATION,

Defendant.

Case No. 8:21-cv-00032

DEFENDANT NOVARTIS PHARMACEUTICALS CORPORATION'S MEMORANDUM IN SUPPORT OF ITS MOTION TO DISMISS THE FIRST AMENDED COMPLAINT

Introduction

The First Amended Complaint should be dismissed as it does not allege sufficient facts to state a plausible claim for relief. *See* Fed. R. Civ. P. 8(a); *Ashcroft v. Iqbal*, 556 U.S. 662 (2009); *Bell Atl. Corp. v. Twombly*, 550 U.S. 544 (2007). The First Amended Complaint fails for three independent reasons. First, plaintiff's claims that Novartis Pharmaceuticals Corporation ("NPC") misrepresented the safety of Beovu® (brolucizumab-dbll) or concealed safety information from its submissions to the Food and Drug Administration ("FDA") (*i.e.*, "fraud-on-the-FDA" claims) are preempted under *Buckman Co. v. Plaintiffs' Legal Committee*, 531 U.S. 341, 352-53 (2001). Second, the FDA-approved Beovu® label has provided notice to physicians about plaintiff's alleged injury since it was first approved in October 2019, and plaintiff fails to allege any relevant "newly acquired information" that would have allowed NPC to change the warnings in the label under applicable regulations prior to plaintiff's January 2020 exposures to Beovu®. Finally, plaintiff's fraud-based claims should be dismissed because they are not pled with particularity.

Background

In this product liability action, plaintiff alleges that NPC failed to warn of "retinal vasculitis, vascular occlusion, and related sequelae"[1] in patients taking Beovu®, a treatment for wet age-related macular degeneration (AMD). AMD is a chronic eye disease characterized by progressive degeneration in the central retina (macula) and is a leading

[1] Plaintiff's First Amended Complaint also refers to "retinal artery occlusion" suggesting that plaintiff's use of the term "retinal vascular occlusion" is used to refer to occlusions of either the arteries or the veins in the retina. *See e.g.*, Filing No. 30 ¶¶ 47, 57, 108, 114.

cause of severe vision loss worldwide.[2] In general, the primary goal of treatment for wet AMD is to slow the ongoing deterioration of visual acuity, which requires drying the retina through the inhibition of new blood vessel growth and reduction of fluid leakage.[3] Beovu® is an important treatment option for patients with wet AMD. Plaintiff alleges she was prescribed Beovu® and it caused her to suffer "retinal vascular occlusion and other sequelae."[4] The complaint asserts four causes of action, all based on claims grounded in failure to warn accusations: (1) strict liability; (2) negligence; (3) fraudulent misrepresentation; and (4) negligent misrepresentation.[5] However, because the Beovu® label at all times contained adequate warnings about the potential for plaintiff's alleged injuries, all of these claims must fail.

The FDA first approved the Biologics License Application (BLA) for Beovu® in October 2019. The initial FDA-approved label ("October 2019 label"), included several warnings about the type of vision deterioration plaintiff alleges in this case.[6] The October

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[2] Approval Package for Beovu® (Sept. 25, 2019), https://www.accessdata.fda.gov/drugsatfda_docs/nda/2019/761125Orig1s000SumR.pdf.

[3] Filing No. 30 ¶ 20.

[4] *Id.* ¶ 13.

[5] *Id.* ¶¶ 79-152.

[6] 2019 Beovu® Label ¶ 6, available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761125s000lbl.pdf. Defendant respectfully requests that the Court take judicial notice of the FDA-approved October 2019 label for Beovu®, pursuant to Federal Rule Evidence 201 (b). Courts routinely take judicial notice of publicly available FDA documents. *Illig v. Union Elec. Co.,* 652 F.3d 971, 976 (8th Cir. 2011) ("In addressing a motion to dismiss, '[t]he court may consider the pleadings themselves, materials embraced by the pleadings, exhibits attached to the pleadings, and matters of public record.'"); *Tierney v. AGA Med. Corp.*, No. 4:11CV3098, 2011 WL 7400469, at *1 (D. Neb. Nov. 18, 2011) (taking judicial notice of publically available FDA documents); *see also Funk v. Stryker Corp.*, 631 F.3d 777, 783 (5th

2019 label included a contraindication for active intraocular inflammation[7] and warnings concerning the potential for various vision injuries in the "Warnings and Precautions" section of the prescribing information.[8] The October 2019 label also describes reports of intraocular inflammation and retinal artery occlusion in patients treated with Beovu® in the "Clinical Trials Experience" section, which lists retinal artery occlusion as an adverse reaction in patients who received treatment with Beovu® during the phase 3 clinical trials.[9] These warnings all preceded plaintiff's two doses of Beovu®.

Despite being exposed to Beovu® on January 21, 2020, and January 30, 2020, plaintiff continually refers to irrelevant information about Beovu® that post-dates her exposures. For example, on February 23, 2020, shortly after FDA's approval of the October 2019 label, but after plaintiff's last of just two total doses of Beovu® on January 30, 2020, the American Society of Retina Specialists (ASRS) provided a statement to its members on reported cases of ocular inflammation occurring since FDA's initial approval.[10] In the statement, the ASRS indicated that it had received reports of vasculitis following Beovu®

Cir. 2011) (district court took appropriate judicial notice of publicly available FDA documents).; *Blankenship v. Medtronic, Inc.*, 6 F. Supp. 3d 979, 984 (E.D. Mo. 2014) (taking judicial notice of FDA records and reports); *see also Becker v. Cephalon*, Inc., No. 14 CIV. 3864, 2015 WL 5472311, at *3 (S.D.N.Y. Sept. 15, 2015) (collecting cases); *Jones v. Medtronic, Inc.*, 411 F. Supp. 3d 521 (D. Ariz. 2019).

[7] *See* 2019 Beovu® Label ¶ 4 (listing three "Contraindications"), https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761125s000lbl.pdf. The 2019 Beovu® label also included contraindications for ocular or periocular infections and hypersensitivity. *Id.*

[8] *Id.* ¶ 5 (listing three "Warnings and Precautions).

[9] *Id.* ¶ 6.1.

[10] Filing No. 30 ¶ 34 (citing ASRS alert to its members).

injection, "11 of which were designated as occlusive retinal vasculitis."[11] Just days later, in March 2020, NPC announced it was "conducting a comprehensive review of a limited number of reported cases of severe vision loss, inflammation and potential retinal vasculitis in patients treated with Beovu®" and that it would also commission an external Safety Review Committee to conduct an independent review of these anecdotal reports of post-market adverse events for Beovu®.[12]

Two months after commissioning an external review (and just seven months after FDA first approved Beovu®), NPC submitted in May 2020 a supplemental biologics license application ("sBLA") to FDA for prior approval to strengthen the "Warnings and Precautions" section of the Prescribing Information.[13] FDA approved NPC's sBLA in June 2020 ("June 2020 label").[14] The "Warnings and Precautions" section of the label was revised to state:

> Retinal vasculitis and/or retinal vascular occlusion, typically in the presence of intraocular inflammation, have been reported with the use of BEOVU [see Contraindications (4.2) and Adverse Reactions (6.1)]. Patients should be instructed to report any change in vision without delay.[15]

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[11] *Id.*

[12] *See Background*, Beovu® (brolucizumab), https://www.brolucizumab.info/overview (last visited Mar. 3, 2021).

[13] Approval Package for Beovu® (June 9, 2020), https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2020/761125Orig1s004ltr.pdf.

[14] *See* 2020 Beovu® Label, https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761125s004lbl.pdf.

[15] Filing No. 30 ¶ 38.

The June 2020 label contains additional information on retinal vascular occlusion in the "Adverse Reactions" section, where intraocular inflammation (defined to include both retinal vasculitis and/or retinal vascular occlusion) is reported as an adverse reaction in patients who received treatment with Beovu® during the phase 3 clinical trials.[16] The June 2020 label's "Patient Counseling Information" section instructs doctors to "[a]dvise patients that in the days following BEOVU administration, patients are at risk of developing endophthalmitis, retinal detachment, retinal vasculitis and/or retinal vascular occlusion."[17] The FDA approval letter in 2019 and updated 2020 label outline the extensive communications between NPC and FDA regarding the Beovu® label.

ARGUMENT

I. Legal Standard

Federal Rule of Civil Procedure 8(a)(2) requires that a complaint contain "a short and plain statement of the claim showing that the pleader is entitled to relief." The Rule "contemplates the statement of circumstances, occurrences, and events in support of the claim presented" and does not authorize a plaintiff's "bare averment that he wants relief and is entitled to it."[18] "[A] plaintiff's obligation to provide the 'grounds' of his 'entitlement to relief' requires more than labels and conclusions, and a formulaic recitation of the elements of a cause of action will not do . . . . Factual allegations must be enough to raise a

[16] *See* 2020 Beovu® Label ¶ 6, https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761125s004lbl.pdf.

[17] *Id.* ¶ 17.

[18] *Twombly*, 550 U.S. at 555 n.3 (2007) (quoting 5 Wright & Miller, Federal Practice and Procedure §1202, at 94, 95).

right to relief above the speculative level[.]"[19] As the Eighth Circuit observed, federal pleading standards have not been satisfied by "plaintiffs who merely parrot the statutory language of the claims that they are pleading (something that anyone could do, regardless of what may be prompting the lawsuit), rather than providing some specific facts to ground those legal claims . . . ."[20] "[T]he pleading standard Rule 8 announces does not require 'detailed factual allegations,' but it demands more than an unadorned, the-defendant-unlawfully-harmed-me accusation."[21]

A complaint is insufficient under Rule 12 where it does not contain sufficient factual allegations to "state a claim to relief that is plausible on its face."[22] A court should first identify and disregard any conclusory allegations because these "are not entitled to the assumption of truth."[23] Next, the court should examine any well-pleaded factual allegations to determine whether those factual allegations "plausibly suggest an entitlement to relief."[24] A plausible cause of action exists only where the facts and theory of liability pled by the plaintiff are not susceptible to an "obvious alternative explanation."[25]

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[19] *Id.* at 555 (internal citations omitted); *see also Iqbal*, 556 U.S. at 681 (When allegations are of a "conclusory nature . . . that disentitles them to the presumption of truth.").

[20] *Barber v. Frakes*, No. 8:20CV282, 2020 WL 6047720, at *3 (D. Neb. Oct. 13, 2020) (citation omitted).

[21] *Iqbal*, 556 U.S. at 678 (internal citations omitted).

[22] *Twombly*, 550 U.S. at 570.

[23] *Iqbal*, 556 U.S. at 679.

[24] *Id.* at 681; *see also Twombly*, 550 U.S. at 555–56.

[25] *Twombly*, 550 U.S. at 567.

II. Federal Regulation of Biologics License Applications

To obtain FDA approval for a new biologics product, a manufacturer must submit a biologics license application ("BLA").[26] A BLA includes, among other things, data from nonclinical laboratory and clinical studies demonstrating that the product meets prescribed requirements for safety, purity, and potency, a full description of manufacturing methods, specifications, data establishing product stability, samples of the product, labeling, and containers, and summaries of product test results.[27]

FDA also closely regulates post-approval changes to FDA-approved biologics' labeling. Manufacturers must notify FDA about "each change in the product, production process, quality controls, equipment, facilities, responsible personnel, or labeling established in the approved license application(s)."[28] FDA can direct a manufacturer to change a BLA's label after it has entered the market,[29] but regulations limit a manufacturer's ability to unilaterally change FDA-approved labels. Specifically, to change prescribing information absent a directive or prior-approval from FDA, a manufacturer must comply with the "changes being effected" (CBE) regulation, set forth at 21 C.F.R. § 601.12(f). That regulation allows manufacturers to change a label without FDA's preapproval only if the changes "'add or strengthen a contraindication, warning,

[26] 21 U.S.C. § 355(b); 42 U.S.C. § 262(a).

[27] 21 C.F.R. §§ 601.2(a); 600.3(kk).

[28] *Id.* § 601.12(a).

[29] *See* 21 U.S.C. § 355(o)(4).

precaution, or adverse reaction" in order to 'reflect newly acquired information.'"[30] "Newly acquired information" is a narrow term defined by regulation as "data, analyses, or other information not previously submitted to the [FDA] . . . if the studies, events, or analyses reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA."[31]

III. Plaintiff's Claims That NPC Misrepresented the Safety of Beovu® or Concealed Safety Information are Preempted.

Central to plaintiff's claims is that NPC misrepresented clinical trial data submitted to FDA in seeking approval for Beovu® (e.g., that the clinical trials failed to accurately report data, and that NPC knew and actively sought to hide such data) and continued to misrepresent or hide this information thereafter. Such "fraud-on-the-FDA" claims are preempted under *Buckman*, 531 U.S. at 352-53. In *Buckman*, the Supreme Court held that a plaintiff's state-law claims based on alleged fraudulent representations made by a manufacturer to obtain approval for orthopedic bone screws were preempted by federal law that empowered FDA to punish and deter fraud perpetrated against it.[32] The *Buckman* Court recognized "[t]he FDCA [Food Drug and Cosmetic Act] leaves no doubt that it is the Federal Government rather than private litigants who are authorized to file suit for noncompliance" with FDCA provisions.[33] The Court explained that Congress has granted FDA "exclusive[]" enforcement authority and "amply empowers the FDA to punish and

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[30] 21 C.F.R. § 601.12(f)(2)(i).

[31] *Id.* § 601.12(f)(6).

[32] *Buckman*, 531 U.S. at 347-52.

[33] *Id.* at 349 n.4 (citing 21 U.S.C. § 337(a) (1990)).

deter fraud against the Administration[.]"[34] Accordingly, private causes of action based on allegations that a sponsor of an FDA-approved product misrepresented information submitted to the FDA are preempted.[35]

While *Buckman* involved claims against the manufacturer of a medical device that was approved by FDA under the Medical Device Amendments ("MDA") of the FDCA, the holding in *Buckman* is not limited to the MDA and is widely applied not only to the FDCA, but to federal agencies other than the FDA.[36] Here, plaintiff's complaint is replete with exactly the types of prohibited allegations discussed in *Buckman* and its progeny, including that NPC "concealed,"[37] "misreport[ed],"[38] "underreported,"[39] and "failed to disclose"[40]

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[34] *Id.* at 348.

[35] *Id.* at 352.

[36] *See, e.g.*, *Lefaivre v. KV Pharm. Co.*, 636 F.3d 935, 944 (8th Cir. 2011) (The Court in Buckman specifically applied field preemption to state-law fraud-on-the-FDA claims because policing fraud against federal agencies "is hardly a field which the States have traditionally occupied.")(citing *Buckman*, 531 U.S. at 347); *Lofton v. McNeil Specialty Pharms.*, 672 F.3d 372 (5th Cir. 2012) (holding plaintiff's claim against drug manufacturer—like plaintiff's claims here—preempted under *Buckman* because it required plaintiff to prove fraud-on-the FDA to recover for failure to warn); *In re Trasylol Products Liability Litigation-MDL-1928*, 763 F. Supp. 2d 1312, 1325 (S.D. Fla. 2010) ("*Buckman* is also implicated where a plaintiff seeks to use a violation of an FDA reporting requirement as proof of negligence."); *Bader Farms, Inc. v. Monsanto Co.*, Case No. 1:16-CV-299 SNLJ, 2017 WL 633815, at *3 (E.D. Mo. Feb. 16, 2017) (whether federal regulatory bodies fulfilled their duties with respect to the entities they regulate is "'inherently federal in character'")(citing *Buckman*, 531 U.S. at 347).

[37] Filing No. 30 ¶¶ 82, 120.a, 144.a.; *see also* ¶¶106, 142 ("concealed, suppressed, or omitted").

[38] *Id.* ¶ 121.

[39] *Id.* ¶ 108.

[40] *Id.* ¶¶ 98.d, 120.a, 144.a.

adverse event reports and other information regarding the safety of Beovu®. These allegations of misrepresentations or omissions in information provided to federal agencies like the FDA are preempted and should be dismissed.

IV. Plaintiff's First Amended Complaint Fails to State a Claim for Relief That Is Plausible on Its Face.

a. Plaintiff fails to state a plausible claim because NPC's FDA-approved label included warnings about plaintiff's alleged injury since its initial approval.

Plaintiff fails to state a claim because NPC's label warned of the injuries alleged at all times and the label is thus adequate as a matter of law.[41] The foundation of plaintiff's First Amended Complaint is that NPC did not warn of "retinal vasculitis, retinal vascular occlusion, and related sequelae."[42] According to plaintiff, "[r]etinal vasculitis is characterized by inflammation" of eye vessels that can lead to "retinal vascular occlusion and/or retinal artery occlusion."[43] However, the plain language of the October 2019 label directly belies this claim. The October 2019 label included a contraindication for active

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[41] *Ideus v. Teva Pharm. USA, Inc.*, 361 F. Supp. 3d 938, 946 (D. Neb. 2019) (Gerrard, J.), *aff'd*, 986 F.3d 1098 (8th Cir. 2021) (holding that label was adequate as a matter of law because it "accurately and unambiguously conveys the scope and nature of the risk"); *Vallejo v. Amgen, Inc.*, No. 8:14CV50, 2014 WL 4922901, at *3 (D. Neb. Sept. 29, 2014) (*citing Felix v. Hoffmann–LaRoche, Inc.*, 540 So.2d 102, 105 (Fla. 1989)) ("while in many instances the adequacy of warnings concerning drugs is a question of fact, it can become a question of law where the warning is accurate, clear, and unambiguous"); *see also Becker*, 2015 WL 5472311, at *6 (stating that "any products liability claim based on a failure-to-warn theory cannot survive in this case because the [] label warns of the very malady allegedly suffered by Decedent"); *Reed v. Pfizer, Inc.*, 839 F. Supp. 2d 571, 576 (E.D.N.Y. 2012) ("[T]he fact (taken here as true) that [plaintiff] suffered from certain conditions that were also identified risks of ingesting [defendant's drug] is tragic, but cannot alone make plausible a claim"); *Trisvan v. Heyman*, 16-CV-00084 (MKB), 2018 WL 6573434, at *3 (E.D.N.Y. Dec. 13, 2018) (same).

[42] Filing No. 30 ¶ 3.

[43] *Id.* ¶ 32.

intraocular inflammation[44] and various warnings concerning potential vision injuries in the "Warnings and Precautions" section of the prescribing information.[45] The October 2019 label also describes reports of intraocular inflammation, retinal artery occlusion, and other vision injuries in patients treated with Beovu® in the "Clinical Trials Experience" section.[46]

In addressing a motion to dismiss, "[c]ourts need not accept as true 'factual assertions that are contradicted by the complaint itself, by documents upon which the pleadings rely, or by facts of which the court may take judicial notice.'"[47] Because the plain language of the October 2019 label contradicts plaintiff's failure-to-warn claims, the Court need not and should not accept those allegations as true.[48] Accordingly, plaintiff's claims should be dismissed for failure to state a viable failure-to-warn claim.[49]

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[44] *See* 2019 Beovu® Label ¶ 4 (listing three "Contraindications"), https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761125s000lbl.pdf.

[45] *Id.* ¶ 5 (listing three "Warnings and Precautions).

[46] *Id.* ¶ 6.1; *see also* June 2020 Beovu® Label ¶ 6.1, https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761125s004lbl.pdf. Defendant respectfully requests that the Court take judicial notice of the FDA-approved October 2019 label for Beovu®, pursuant to Federal Rule Evidence 201 (b). *See also supra* n.6.

[47] *Willstrop v. Prince Mktg. LLC*, 8:17CV350, 2018 WL 3201888, at *3 (D. Neb. Feb. 15, 2018) (citations omitted).

[48] *Cohen v. United States,* 129 F.2d 733 (8th Cir. 1942) (finding that the court need not accept as true those factual allegations which "appear by a record or document included in the pleadings to be unfounded"); *see also Kaempe v. Myers,* 367 F.3d 958, 963 (D.C. Cir. 2004) ("Nor must we accept as true the complaint's factual allegations insofar as they contradict exhibits to the complaint or matters subject to judicial notice.").

[49] Fed. R. Civ. P. 12(b)(6).

b. Plaintiff fails to allege "newly acquired information" that would trigger the CBE exception to preemption.

Plaintiff's amended pleading reveals why she failed to include her date of exposure in her initial complaint—she received Beovu® long before all but one of the articles or commentaries on which she relies so heavily in her complaints. Plaintiff now admits that she received Beovu® on January 21, 2020 and January 30, 2020. Her First Amended Complaint, however, references numerous papers published after those exposures.[50] In the context of a motion to dismiss, a plaintiff must allege "newly acquired information" that would trigger the applicability of the CBE regulation.[51] Only after Plaintiff has pleaded such facts will the court consider whether a defendant met its own burden to demonstrate by "clear evidence" that the FDA would not have approved the labeling change.[52] Plaintiff's

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[50] *See e.g.,* Filing No. 30 ¶ 30 (citing April 25, 2020 publication); ¶ 34 (citing February 23, 2020 alert issued by the American Society of Retina Specialists); ¶ 35 (citing March 30, 2020 alert issued by the American Society of Retina Specialists); ¶¶ 42-69 (citing information published *after* plaintiff's last exposure).

[51] *Ideus v. Teva Pharm. USA, Inc.*, No. 4:16-CV-3086, 2017 WL 6389630, at *3 (D. Neb. Dec. 12, 2017) (Gerrard, J.); *see also In re Celexa and Lexapro Mktg. and Sales Prac. Litig.*, 779 F.3d 34, 43 (1st Cir. 2015) (holding inadequate-warning based pharmaceutical drug claims preempted at motion-to-dismiss stage); *Gibbons v. Bristol-Myers Squibb Co.*, 919 F.3d 699, 708 (2d Cir. 2019) ("[T]o state a claim for failure-to-warn that is not preempted by the FDCA, a plaintiff must plead 'a labeling deficiency that [Defendants] could have corrected using the CBE [Changes Being Effected] regulation.'"); *Utts v. Bristol-Myers Squibb Co.*, 251 F. Supp. 3d 644, 672-63 (S.D.N.Y. 2017), *aff'd*, 919 F.3d 699 (2d Cir. 2019) ("It is well-established that preemption may be analyzed and decided at the motion to dismiss stage."); *PLIVA, Inc. v. Mensing*, 564 U.S. 604, 624 (2011) (same); *Mitchell v. Boehringer Ingelheim Pharm.*, No. 1:16-cv-02384-STA-egb, 2017 WL 5617473 (W.D. Tenn. 2017).

[52] *Gibbons*, 919 F.3d at 708; *Mahnke v. Bayer Corp.*, Case No. 2:19-cv-07271-RGK-MAA, 2019 WL 8621437, at *3 (C.D. Cal. Dec. 10, 2019) (citing *Gibbons*, 919 F.3d at 708). *See also D'Agnese v. Novartis Pharms. Corp*., 952 F. Supp. 2d 880, 892 (D. Ariz. 2013) (stating that claims based on inadequate warnings must be based on what was knowable at the time a warning should have allegedly been given).

references to various information post-dating her exposure cannot constitute "newly acquired information" that would have justified a pre-exposure label change under the CBE regulations.

"The CBE procedure is only available to make changes . . . based on 'newly acquired information'" discovered after a label receives initial FDA approval.[53] Newly acquired information" is defined by regulation as:

> "[D]ata, analyses, or other information not previously submitted to the [FDA] which may include (but are not limited to) data derived from new clinical studies, reports of adverse events, or new analyses of previously submitted data (e.g., meta-analyses) if the studies, events, or analyses reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA."[54]

That means plaintiff must allege facts showing "some indication of 'newly acquired information' as to trigger the applicability of the CBE regulation" *before their exposure to Beovu®* to escape preemption.[55]

In *Mahnke*, plaintiff alleged that the defendant failed to adequately warn of the risks associated with Magnevist on the product's label, specifically, that the label should have warned of the risk of gadolinium retention prior to plaintiff's 2015 exposure to Magnevist.[56] Defendants moved to dismiss and the court considered whether plaintiff met its burden of alleging facts that the defendant could have unilaterally changed a label

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[53] *In re Celexa*, 779 F.3d at 41–42 (emphasis added).

[54] 21 C.F.R. § 601.12(f)(6).

[55] *E.g., Ideus*, 2017 WL 6389630, at *2.

[56] *Mahnke*, 2019 WL 8621437, at *3–4.

because of newly acquired information.[57] Specifically, the court considered whether a 2018 review paper and papers discussing gadolinium retention warranted use of the CBE regulation.[58] The court held that neither is sufficient to meet plaintiff's burden. Regarding the 2018 review paper, the court found that it was insufficient to show that defendant could have invoked the CBE regulation because it "was published outside of the relevant time frame" (i.e., it was published after plaintiff's 2015 exposure).[59] The court further found that the pre-exposure papers cited in plaintiff's complaint were insufficient on their face to constitute "newly acquired information" because they failed to show a causal association between gadolinium retention and a clinically significant adverse reaction.[60] Instead, as the court notes, these papers stated that the clinical significance of gadolinium retention was unknown.[61] As such, plaintiff's claims were preempted as a matter of law for failure to adequately plead relevant "newly acquired information" that would have enabled defendant to change its label under the CBE regulations.

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[57] *Id.*

[58] *Id.* at *4.

[59] *Id.*

[60] *Id.*

[61] *Id.* The court also considered plaintiff's argument made in opposition to the motion to dismiss that defendant should have "pieced together" recent research to conclude that gadolinium is toxic. *Id.* The court rejected plaintiff's argument because plaintiff's conclusory allegation was unsupported and plaintiff identified no newly acquired information showing a causal association between gadolinium retention and a clinically significant adverse reaction. *Id.*

Similarly, in *Sabol*, plaintiff alleged that the defendant failed to adequately warn of the risks associated with Magnevist (i.e., gadolinium retention).[62] Defendants moved to dismiss and the court considered whether plaintiff met its burden of alleging sufficient newly acquired information.[63] The court considered two pre-exposure studies cited in the amended complaint.[64] After reviewing the studies, the court concluded that neither provided "reasonable evidence" of a causal relationship between gadolinium retention and adverse events.[65] The court found that the first study did not involve a clinically significant adverse reaction and that the second study was insufficient because it was "not clear what relationship, causal or otherwise, this study" drew between gadolinium retention and adverse reactions. As such, the court held that plaintiff failed to adequately plead newly acquired information.[66]

Here, like the plaintiffs in *Mahnke* and *Sabol*, plaintiff fails to state a claim for relief that is plausible on its face that *prior* to her exposure, NPC could have unilaterally changed the label without FDA approval based on "newly acquired information." Plaintiff alleges that she was prescribed and injected with Beovu® on January 21, 2020 and January 30, 2020. Plaintiff's First Amended Complaint references only two pieces of information between the initial October 2019 FDA approval and her January 30, 2020 injection: (1)

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[62] *Sabol v. Bayer Healthcare Pharm., Inc.*, 439 F. Supp.3d 131, 136 (S.D.N.Y. 2020).

[63] *Id*.

[64] *Id.* at 148.

[65] *Id.*

[66] *Id.* at 149-51. The court also disregarded as insufficient studies of rats as they are "not sufficient to demonstrate that a risk to humans is apparent." *Id.* at 149-50.

anecdotal post-market reports of retinal vascular occlusion;[67] and (2) a January 17, 2020 online publication in the Journal of Ophthalmology.[68] These unanalyzed adverse event reports do not "reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA."[69] Nor does plaintiff allege as much.[70] In fact, the FDA was aware of reports of retinal occlusion in patients taking Beovu® due to that information being explicitly included in the initial October 2019 FDA-approved Beovu® label. As such, these few adverse event reports do not represent new evidence of a different type or greater severity or frequency than previously included in NPC's submissions to the FDA.

Even if these adverse event reports purported to show a difference in severity or frequency, they do not demonstrate the causal association required to be considered newly acquired information. In order to qualify as "newly acquired information," the information must demonstrate "reasonable evidence of a causal association with a drug."[71] "The fact that a user of a drug has suffered an adverse event, standing alone, does not mean that the

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[67] Filing No. 30 ¶¶ 70-73 (citing 12 alleged adverse event reports occurring before January 30, 2020 (plaintiff's last exposure to Beovu®)).

[68] Filing No. 30 at ¶ 66 (citing Nguyen et al., *Brolucizumab: evolution through preclinical and clinical studies and the implications for the management of neovascular age-related macular degeneration*, American Academy of Ophthalmology Vol. 127, No. 7 (July 2020) (available online Jan. 17, 2020).

[69] 21 C.F.R. § 601.12(f)(6).

[70] *See* Filing No. 30 ¶¶ 70-73.

[71] 21 C.F.R. § 201.57(c)(6)(i).

drug caused that event."[72] Adverse event reports are anecdotal descriptions of something happening after a person receives a drug therapy; on their face, they do not even purport to reach any conclusions regarding a causal association. Plaintiff herself could submit an adverse event report to FDA. Due to their anecdotal nature, both the FDA and courts analyzing failure-to-warn claims like plaintiff's here routinely hold that such reports cannot be treated as reliable evidence of causation. "Under a plain reading of the regulations, adverse event reports, without any analysis indicating causality, cannot constitute 'newly acquired information.'"[73] Even "[r]eports and studies that discuss" adverse events—much less the reports standing alone—are not "newly acquired information."[74] Plaintiff's

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[72] *Matrixx Initiatives, Inc. v. Siracusano*, 563 U.S. 27, 44 (2011).

[73] *Gayle v. Pfizer Inc.*, 2020 WL 1685313, at *5 (S.D.N.Y. April 7, 2020) (finding that 6,000 adverse event reports showing type 2 diabetes in patients that took cholesterol did not amount to a causal association and thus, was not newly acquired information); *id.* (concluding that unanalyzed adverse event reports "miss[] the mark," where plaintiff "offer[s] no analysis" and "merely proffer the adverse event reports by themselves."); *see also Utts*, 251 F. Supp.3d at 664 (stating that "sheer numbers of case reports . . . reveal little about how frequently the events occur in the broader patient population."). *See also Rider v. Sandoz Pharm. Corp.*, 295 F.3d 1194, 1199 (11th Cir. 2002) (affirming district court's conclusion that case reports did not by themselves provide reliable proof of causation); *Hollander v. Sandoz Pharm. Corp.*, 289 F.3d 1193, 1211 (10th Cir. 2002) (finding district court did not abuse its discretion in finding case reports unreliable under *Daubert*); *Glastetter v. Novartis Pharm. Corp.*, 252 F.3d 986, 989-90 (8th Cir. 2001) (affirming district court's holding that case reports are not scientifically valid proof of causation). *See also* 21 C.F.R. § 600.80(n) (stating that for postmarketing reporting of adverse experiences a "report or information submitted by an applicant under this section (and any release by FDA of that report or information) does not necessarily reflect a conclusion by the applicant or FDA that the report or information constitutes an admission that the biological product caused or contributed to an adverse effect."); FDA, *Questions and Answers on FDA's Adverse Event Reporting System (FAERS)* (June 4, 2018) (stating that the "[e]xistence of a[n] [adverse event] report does not establish causation"), available at https://www.fda.gov/drugs/surveillance/questions-and-answers-fdas-adverse-event-reporting-system-faers.

[74] *McGrath v. Bayer Healthcare Pharm.*, 393 F. Supp.3d 161, 169 (E.D.N.Y. June 24, 2019) (holding that "[r]eports and studies that . . . do not reach any conclusions regarding

reference to a few adverse event reports, therefore, does not constitute "newly acquired information" that can save her claims from preemption.

Second, an online publication that merely reviews clinical trial data that was previously submitted to the FDA does not constitute newly acquired information.[75] And plaintiff does not allege that the January 17, 2020, online publication purports to reanalyze the previously submitted data.[76] Moreover, plaintiff does not allege that this online publication purports to either "reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA"[77] or demonstrate "reasonable evidence of a causal association with a drug."[78] Plaintiff's reference to this online publication thus does not constitute an allegation of "newly acquired information" that might allow her to escape preemption under the CBE regulations.[79]

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the adverse effects or risks" of a product cannot be "newly acquired information" that could support a going ahead with a CBE warning change); *see also Sabol*, 439 F. Supp.3d at 149 ("a tentative, at best, suggestion of a causal relationship" cannot "support[] the inference" of "a clinically significant adverse reaction that would require a manufacturer to change its label"); *but see Stube v. Pfizer Inc.*, 446 F. Supp. 3d 424 (W.D. Ark. 2020) (holding that plaintiffs sufficiently *alleged* newly acquired information when plaintiffs pointed to 47,287 adverse event reports along with several medical studies and trials).

[75] 21 C.F.R. § 601.12(f)(6) (emphases added) (defining newly acquired information as "data, analyses, or other information ***not*** previously submitted to the [FDA]").

[76] Filing No. 30 ¶ 66; *see also* 21 C.F.R. § 601.12(f)(6) (emphases added) (defining newly acquired information as "new analyses of previously submitted data (e.g., meta-analyses) if the studies, events, or analyses reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA.").

[77] 21 C.F.R. § 601.12(f)(6).

[78] 21 C.F.R. § 201.57(c)(6)(i).

[79] Plaintiffs state that the authors "admit to the causal relationship between Beovu and the injuries complained of herein." Filing No. 30 ¶ 66. But that statement is irrelevant to the Court's determination—it was based on information (and was published) after plaintiff's

In sum, the First Amended Complaint provides no basis upon which the Court could conclude that the adverse event reports or online publication presented either a different type or more severe risk than those the company had discussed with FDA or reasonable evidence of causation.[80]

V. Plaintiff's Fraud-Based Claim Should Be Dismissed Because It Is Not Pled With Particularity.

Plaintiff's fraudulent misrepresentation claim is subject to the heightened pleading standard in Fed. R. Civ. P. 9 (b), requiring her to state with particularity the circumstances constituting fraud or mistake.[81] Rule 8 does not empower a plaintiff to plead the bare elements of her cause of action, affix the label "general allegation," and expect the complaint to survive a motion to dismiss.[82] In cases concerning fraudulent misrepresentation and omission of facts, Rule 9(b) typically requires the pleading to

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final exposure to Beovu®. *Ideus*, 2017 WL 6389630, at *3 (stating that the relevant time period is after label approval but before exposure); *see also Mahnke*, 2019 WL 8621437, at *3-4 (finding that a review paper published after plaintiff's exposure was "insufficient to show that [defendant] could have invoked the CBE regulation."); *Sabol*, 439 F. Supp.3d at 148 n.13 (stating that "[t]he Court will disregard the many articles cited in the Amended Complaint that were published after [plaintiff's] last [use of the product]. These studies can have no bearing on her failure-to-warn claim."); *Ridings v. Maurice*, 444 F. Supp.3d 973, 993 (W.D. Mo. Mar. 16, 2020) ("[S]tudies published after a plaintiff's injury [are not] relevant to constitute newly acquired information.").

[80] *See, e.g.*, *Gibbons*, 919 F.3d at 708 (affirming district court's dismissal of complaint alleging that defendants became aware of "many reports of serious hemorrhaging in users of [their] drugs" and that "[n]umerous… studies published after Eliquis' approval in 2012 confirm the problematic bleeding events[.]").

[81] *See Iqbal*, 556 U.S. at 686 (discussing the elevated Rule 9(b) pleading standard). Courts in this Circuit have also applied Rule 9(b) pleading requirements to plaintiff's negligent misrepresentation claim. *See e.g., Arroyo v. Wheat*, 591 F. Supp. 136 (D. Nev. 1984) (court applied Rule 9(b) pleading requirements to negligent misrepresentation claim).

[82] *Iqbal*, 556 U.S. at 687.

include "such matters as the time, place, and contents of false representations, as well as the identity of the person making the misrepresentation and what was obtained or given up thereby."[83] Simply put, plaintiff must state "the who, what, when, where, and how" of the alleged fraud.[84] With regard to intent, plaintiff must plead facts plausibly indicating that NPC intended to deceive her. "[C]onclusory allegations that a defendant's conduct was fraudulent and deceptive are not sufficient to satisfy the rule."[85] To prove fraudulent misrepresentation under Nebraska law, a plaintiff must allege: "(1) that a representation was made; (2) that the representation was false; (3) that when made, the representation was known to be false or made recklessly without knowledge of its truth and as a positive assertion; (4) that [the representation] was made with the intention that the plaintiff should rely upon it; (5) that the plaintiff reasonably did so rely [on it]; and (6) that the plaintiff suffered damage as a result."[86]

Here, the First Amended Complaint fails to state a claim for fraudulent misrepresentation because plaintiff only alleges conclusory allegations of fraud and has failed to plead any ultimate facts to show that her injury resulted from her reliance on any of NPC's purported falsehoods. The First Amended Complaint fails to specify where or when the alleged false statements were made to plaintiff; fails to elaborate on the exact substance of the alleged falsehoods; fails to allege who made the statements; and fails to

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[83] *Bennett v. Berg*, 685 F.2d 1053, 1062 (8th Cir. 1982).

[84] *Chaney v. Evnen*, 307 Neb. 512, 524-25 (2020).

[85] *Com. Prop. Inv., Inc. v. Quality Inns Int'l, Inc.*, 61 F.3d. 639, 644 (8th Cir. 1995).

[86] *Cao v. Nguyen*, 258 Neb. 1027, 1031 (2000).

explain what the alleged falsehoods caused her to do (or not do).[87] Plaintiff makes only vague and conclusory misrepresentation allegations—i.e., that NPC through "labeling, advertising, product inserts, promotional materials, or other marketing" represented that Beovu® was safe and effective—which it is—but does not provide any specific facts required to support allegations that those representations were fraudulent.[88] For example, plaintiff fails to identify which advertisements, marketing, or promotions allegedly contain misrepresentations; which safety statements are wrong; and when any of these statements were made. Plaintiff also fails to allege with specificity any facts to show how she relied on any of NPC's statements.[89]

Plaintiff fails to state the "what" or the "how" but instead makes generalized allegations of NPC's alleged false statements "to induce consumers and the medical community, *including Plaintiff and Plaintiff's healthcare providers*, to use, prescribe, and purchase Beovu."[90] Plaintiff does not allege "what" or "when" NPC made "misrepresentations" to her healthcare provider that were then relied on or "how" the

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[87] *See Brummels v. Tomasek*, 273 Neb. 573, 731 N.W.2d 585 (2007) (overruled on other grounds by, *Knights of Columbus Council 3152 v. KFS BD, Inc.*, 280 Neb. 904, 791 N.W.2d 317 (2010)) (plaintiff failed to state a claim because he failed to allege that the defendants made false representations to him (an element of fraudulent misrepresentation)).

[88] *See e.g.,* Filing No. 30 ¶¶ 135, 149. NPC believes, consistent with the data, that Beovu® is safe and effective.

[89] *See Malone v. Kantner*, No. 4:12-CV-3190, 2014 WL 2858246, at *5 (D. Neb. June 23, 2014) ("More importantly, unlike intent, reliance must be pleaded with particularity.") (citing *In re NationsMart Corp. Sec. Litig.*, 130 F.3d 309, 321-22 (8th Cir. 1997)).

[90] Filing No. 30 ¶ 106 (emphasis added).

provider was "induced" to prescribe Beovu®.[91] Plaintiff not only fails to specify the same regarding her reliance on the "misrepresentations," but plaintiff never alleges that she is a healthcare provider that used, prescribed, or purchased Beovu® so she clearly was not "induced" into such activities.[92] Plaintiff fails to allege that she relied upon NPC's purportedly erroneous statements, thus the First Amended Complaint omits an element that is required for a fraudulent misrepresentation.[93] Because plaintiff's fraudulent misrepresentation claim falls well short of establishing specific facts that, if true, would establish a viable fraudulent misrepresentation claim against NPC, the Court should dismiss the claim on that basis as well.

CONCLUSION

For the foregoing reasons, the Court should grant this motion and dismiss the First Amended Complaint in its entirety.

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[91] *See Zaccarello v. Medtronic, Inc.*, 38 F. Supp. 3d 1061, 1071 (W.D. Mo. 2014) ("Plaintiff's allegations do not satisfy this standard. Plaintiff provides detailed allegations on studies, journal articles, investigations, and media reports, but he fails to identify (among other things) the particular misrepresentations and knowingly false statements that were made to him and his physician.").

[92] *See* Filing No. 30 ¶ 13 (stating date of administration of Beovu®).

[93] *See Lucky 7, L.L.C. v. THT Realty, L.L.C.*, 278 Neb. 997, 1003 (2009) ("[N]o recovery for fraudulent misrepresentation, fraudulent concealment or negligent misrepresentation is possible unless plaintiffs can prove justifiable reliance, i.e., that any reliance was reasonable.").

Dated: April 13, 2021

Respectfully submitted,

NOVARTIS PHARMACEUTICALS CORPORATION, Defendant.

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CERTIFICATE OF COMPLIANCE WITH NECivR 7.1(d)(4)

I hereby certify that the Defendant Novartis Pharmaceuticals Corporation's Memorandum in Support of its Motion to Dismiss the First Amended Complaint (Filing No. 34) complies with the type-volume limitations of NECivR 7.1(d)(4) because it contains 6,550 words. This word count includes all text, including the caption, headings, footnotes, and quotations. I have relied on Microsoft Office Home and Business 2019-word processing software used to prepare the memorandum for the statement of word count.

/s/Michael K. Huffer